

## ABSTRACT

A signal amplification system comprises a bacterial multi-hybrid system, and more preferably a two-hybrid system, of at least two chimeric polypeptides containing a first chimeric polypeptide corresponding to a first fragment of an enzyme and a second chimeric polypeptide corresponding to a second fragment of an enzyme or a modulating substance capable of activating said enzyme. The first fragment is fused to a molecule of interest and the second fragment or the modulating substance is fused to a target ligand. The activity of the enzyme is restored by the *in vivo* interaction between the molecule of interest and the target ligand. Signal amplification is generated and, for example, triggers transcriptional activation. The signal amplification system is useful in a method of selecting a molecule of interest, which is capable of binding to target ligand, wherein the interaction between the molecule of interest and the target ligand is detected with the signal amplification system as a kit therefor. A method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest is also provided.